REMARKS

Claims 1, 2, 7, 9-13, 17-19, 22-24, 27, and 39-46 are currently pending in the above-identified application, with claims 28-33 not being considered as pending by the Examiner. Applicant has hereinabove canceled claims 2, 10, 22, 28-33, 42, and 44 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or other application. In addition, applicant has amended claims 1, 9, 11-13, 17, 18, 27, and 39, and added new claims 47 and 48. Applicant maintains that this Amendment raises no issue of new matter. Support for the amendments to claim 1 can be found in the specification at, *inter alia*, page 6, lines 2-8 and 14-15. Support for the amendments to claim 2 can be found in the specification at, *inter alia*, page 6, lines 10-12. Support for the amendments to claims 9 and 11 can be found in the specification at, *inter alia*, page 13, lines 7-18. Support for the amendments to claims 12 and 13 can be found in the specification at, *inter alia*, page 13, lines 20-25. Support for the amendments to claim 17 can be found in the specification at, *inter alia*, page 14 lines 19-33 and 34-35; page 10, lines 12-17; page 23, lines 7-15; page 27, lines 19-31; page 29, line 34 to page 30, line 7; and in Figure 3e. Support for the amendments to claim 18 can be found in the specification at, *inter alia*, page 17, line 35 and page 14, line 34 to page 15, line 2. Support for the amendments to claim 27 can be found in the specification at, *inter alia*, page 6, lines 2-8, and page 9, lines 7-15. Support for the amendments to claim 39 can be found in the specification at, *inter alia*, page 6, lines 2-8, and page 9, lines 18-26. Support for new claim 47 can be found in the specification at, *inter alia*, page 6, lines 2-8; page 14 lines 19-33 and 34-35; page 23, lines 7-15; page 27, lines 19-31; page 29, line 34 to page 30, line 7; and in Figure 3e. Support for new claim 48 can

be found in the specification at, *inter alia*, page 6, lines 2-8; page 14 lines 19-33 and 34-35; page 9, lines 4-16; page 10, lines 12-17; page 23, lines 7-15; page 27, lines 19-31; page 29, line 34 to page 30, line 7; and in Figure 3e. Accordingly, applicant respectfully requests entry of this Amendment. After entry of this Amendment, claims 1, 9, 11-13, 17-19, 23, 24, 27, 39, 43, and 45-48 will be pending and under examination.

In the August 18, 2003 Final Office Action, the Examiner stated that the numbering of claims is not in accordance with 37 C.F.R §1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. The Examiner stated that when claims are canceled, the remaining claims must not be renumbered. The Examiner stated that when new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). The Examiner further stated that the amendment filed 5-12-03 added claims 28-38 but only claims 34-38 are shown in the text that followed. The Examiner stated that however, in the marked version (unofficial) of the amended claims, claims 28-38 are shown. The Examiner stated that the amendment filed 6-13-03 indicates that new claims 34-38 were mistakenly referred to as new claims 28-38 and the new claims 34-38 have been canceled, and the pending claims are 1, 2, 7, 9-13, 17-19, 22-24, 27 and 39-46. The Examiner stated that therefore, claims 28-38, which apparently are duplicates of claims 39-44, will not be considered pending claims in the present Official action. The Examiner stated that cancellation of claims 28-33 is required.

In response, applicant has hereinabove canceled claims 28-33 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or other application.

Claims Reject d Under 35 U.S.C. §112, First Paragraph

The Examiner stated that claims 17-19 and 22-24 remain rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention and is repeated for the reason set forth in the preceding Official Action mailed 11-7-02 (Paper No.21). The Examiner also stated that applicant's arguments filed 5-12-03 and 6-13-03 have been fully considered but they are not persuasive. The Examiner further stated that applicant cites specification page 14, lines 19-32, page 23, lines 7-15, page 27, lines 19-31, and page 29, lines 34 to page 30, line 7 and argue that when read together the specification has support for a method of determining whether a compound increases incidence of ICH with or without the presence of said compound (amendment, p.9). The Examiner stated that this is not found persuasive because of the reasons set forth in the preceding Official Action mailed 11-7-02 (Paper No. 21). The Examiner stated that the specification page 23, lines 7-15, page 27, lines 19-31, and page 29 lines 34 to page 30, line 7 disclose an ICH assay and compare the effect of CD39 and aspirin on the incidence of ICH but fail to provide support for comparing the incidence of ICH with or without the presence of CD39. The Examiner stated that, further, there is no nexus between no increase of the incidence of ICH and capability of a compound of treating or preventing the thrombotic of ischemic disorder in a subject. The Examiner stated that, thus, claims 17-19 and 22-24 remain rejected under 35 U.S.C. §112, first paragraph.

In response, applicant respectfully traverses the Examiner's rejection. Applicant maintains that the claimed subject matter is

adequately described in the specification. More specifically, applicant notes that, in addition to the support cited by applicants previously, Figure 3e of the specification shows a comparison of intracerebral hemorrhage with and without CD39 (vehicle), i.e. in the absence of presence of CD39.

In addition, applicants maintain that the nexus between treating stroke and not increasing intracerebral hemorrhage is clearly described in the specification. Specifcally, the claimed subject matter is directed to testing compounds for determining if they are capable for treating thrombotic disorders, and the requirement that such compounds not increase incidence of intracerebral hemorrhage is cited throughout the specification, e.g. see page 2, lines 15-18, which otherwise can render the compound unsuitable for treating thrombotic disorders, e.g. see page 2, lines 4 to 6. In short, a test which determines if compound both decreases platelet deposition and does not increase the incidence of intracerebral hemorrhage indicates that the compound is capable of treating the thrombotic disorder in the subject.

Accordingly, applicant maintains that the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §112, First Paragraph

The Examiner stated that claims 1, 2, 7, 9-13 and 27 remain rejected and claims 40 and 41 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling of the use of soluble CD39 in the treatment and prevention of

thrombotic and ischemic disorders in mice and BIBU52 in rhesus and marmoset monkeys (Guth et al., abstract), does not reasonably provide enablement for the use of an active fragment of CD39 comprising amino acid 1-50 of SEQ ID No.2 or about 20-80 amino acid of SEQ ID No.1 that mimics the active site, or for the use of any deletion mutant, insertion mutation, or any truncated mutant of CD39 polypeptide for treating or preventing stroke in a subject. The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 11-7-02 (Paper No.21). The Examiner stated that applicant's arguments filed 5-12-03 and 6-13-03 have been fully considered but they are not persuasive. The Examiner stated that claims 40 and 41 are directed to a method for treating preventing stroke in a human subject by using a deletion mutant of the CD39 polypeptide, comprising amino acid sequence of SEQ ID No.2, which lacks a transmembrane domain (TMD), or a CD39 polypeptide comprising amino acids 1-50 or SEQ ID No. 2.

The Examiner stated that applicant argues that the teaching of Schutle et al. are not relevant to the clamed invention because the claims do not recite using a CD39 variant contained a FLAG-tag or a GPI anchor and synthesizing polypeptide fragment and identification of therapeutic fragment do not requite undue experimentation (amendment, p.14). The Examiner stated that this not found persuasive because of the reasons set forth in the preceding Official Action mailed 11-7-02 (Paper No. 21). The Examiner stated that Schulte teaches that apyrase conserved regions (ACR)-1, -4, and -5 within CD39 polypeptide are required for maintenance of biochemical activity of the CD39 polypeptide (e.g. abstract). The Examiner stated that therefore, a CD39 polypeptide mutant must comprise ACR-1, -4, and -5 in order to

maintain its biochemical activity so as to treat or prevent stroke in mice or a subject. The Examiner stated that the claims encompass using CD39 polypeptide comprising amino acids 1-50 of SEQ ID NO:2 or about 20-80 amino acids of SEQ ID NO:1 that mimics the active site, or any deletion mutant, such as deletion of TMD, insertion mutant any truncated mutant of CD39 polypeptide for treating and preventing stroke in a subject. The Examiner stated that the term "comprising" is an open language term and means adding any amino acid sequence, including FLAG-tag or CPI anchor, onto 5' and/or 3' end of the core amino acid sequence. The Examiner stated that, further, the presence of FLAG-tag is to ensure membrane expression of the protein and does not seem to interfere with the biological activity of CD39 polypeptide. The Examiner stated that thus, the teachings of Schutle et al. are relevant to the claimed invention.

The Examiner stated that as discussed in the preceding Official action mailed 11-7-02 (Paper No. 21), amino acid sequence of a protein determines is structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. The Examiner stated that although method of synthesizing polypeptide fragments was known, protein function was unpredictable from mere amino acid sequence at the time of the invention, therefore, it would require undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed.

In response, applicant respectfully traverses the Examiner's rejection. Applicant maintains that the claimed subject matter is fully enabled by the specification. More specifically, claims 1

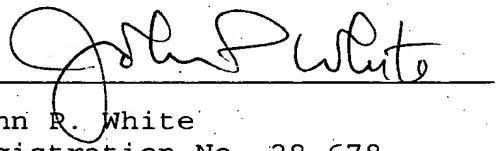
and 27 as amended do not recite mutants or fragments of the CD39 polypeptides, but recite SEQ ID NOs:1 and 2, as present in the specification at page 9, lines 7 to 26. Furthermore, both of the sequences recited contain the ACRs cited by Schulte. In addition, applicants have added new claims 47 and 48. The fragment or mutant of CD39, as recited in claims 47 and 48 respectively, is further characterized as able to decrease platelet deposition without increasing incidence of intracerebral hemorrhage as particularized in the specification and recited in the claim support hereinabove. Applicants maintain that although some routine experimentation may be required, the experimentation is clearly not undue experimentation and is clearly enabled by the working example in the specification, at for example page 25, line 25 to page 27 line 16; page 6, lines 2-8; page 14 lines 19-33; page 23, lines 7-15; page 27, lines 19-31; page 29, line 34 to page 30, line 7; page 9, lines 4-16; page 10, lines 12-17; and in Figure 3e. Applicant notes that, with respect to the Examiner's argument and the new claim 47 and 48, there is no need for prediction of protein function from the amino acid sequence.

Accordingly, for the reasons set forth hereinabove, the applicant maintains that the claimed subject matter is fully enabled by the specification, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed total fee of $141.00 including a $55.00 fee for a one month extension of time and $86.00 claim fees, is deemed necessary in connection with the filing of this Amendment. If any such fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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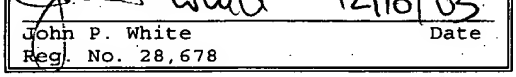

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John P. White — Date
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